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Figure 4

FIX 176834 RACE_95_3 RACE_95_8 RACE_95_11	-GTCTGCAACATGCGGCTGTGTCGGGTGTGGCTGTCTGTTTGTCTGTGCGCCGTGGTG
FIX	GGTCAGTGCCAGCGGGAGACCGCAGAAAAAAA CGATTATTACCGAGTACCGCATTACT
RACE_95_3	GGTCAGTGCCAGCGGGAGACCGCAGAAAAAA CGATTATTACCGAGTACCGCATTACT
RACE_95_8	GGTCAGTGCCAGCGGGAGACCGCAGAAAAAAA CGATTATTACCGAGTACCGCATTACT
RACE_95_11	GGTCAGTGCCAGCGGGAGACCGCAGAAAAAAA
FIX	GGGACGCGTGCTCTCGCGCGCTGCCTGACCAAACCCGTTACAAGTATGTGGAACAGCTCG
RACE_95_3	GGGACGCGTGCTCTCGCGCGCTGCCTGACCAAACCCGTTACAAGTATGTGGAACAGCTCG
RACE_95_8	GGGACGCGTGCTCTCGCGCGCTGCCTGACCAAACCCGTTACAAGTATGTGGAACAGCTCG
RACE_95_11	GGGACGCGTGCTCTCGCGCGCTGCCTGACCAAACCCGTTACAAGTATGTGGAACAGCTCG
FIX RACE_95_3 RACE_95_8 RACE_95_11	TGGACCTCACGTTGAACTACCACTACGATGCGAGCCACGGCTTGGACAACTTTGACGTGC TGGACCTCACGTTGAACTACCACTACGATGCGAGCCACGGCTTGGACAACTTTGACGTGC TGGACCTCACGTTGAACTACCACTACGATGCGAGCCACGGCTTGGACAACTTTGACGTGC TGGACCTCACGTTGAACTACCACTACGATGCGAGCCACGGCTTGGACAACTTTGACGTGC
FIX	TCAAGAGGTGAGGGTACGCGCTAAAGGTGTATGACAACGGGAAGGTAAGGGCGAACGGGT
RACE_95_3	TCAAGAG
RACE_95_8	TCAAGAGGTGAGGGTACGCGCTAAAGGTGTATGACAACGGGAAGGTAAGGGCGAACGGGT
RACE_95_11	TCAAGAG
FIX RACE_95_3 RACE_95_8 RACE_95_11	AACGGGTAGGTAACCGCATGGGGTGTGAAATGACGTTCGGAACCTGTGCTTGCAGAATCA
FIX	ACGTGACCGAGGTGTCGTTGCTCATCAGCGACTTTAGACGTCAGAACCGTCGCGGCGGCA
RACE_95_3	ACGTGACCGAGGTGTCGTTGCTCATCAGCGACTTTATACGTCAGAACCGTCGCGGCGGCA
RACE_95_8	ACGTGACCGAGGTGTCGTTGCTCATCAGCGACTTTAGACGTCAGAACCGTCGCGGCGGCA
RACE_95_11	ACGTGACCGAGGTGTCGTTGCTCATCAGCGACTTTAGACGTCAGAACCGTCGCGGCGCA
FIX	CCAACAAAAGGACCACGTTCAACGCCGCCGGTTCGCTGGCGCCTCACGCCCGGAGCCTCG
RACE_95_3	CCAACAAAAGGACCACGTTCAACGCCGCCGGTTCGCTGGCGCCTCACGCCCGGAGCCTCG
RACE_95_8	CCAACAAAAGGACCACGTTCAACGCCGCCGGTTCGCCGCCTCACGCCCGGAGCCTCG
RACE_95_11	CCAACAAAAGGACCACGTTCAACGCCGCCGGTTCGCTGGCGCCTCACGCCCGGAGCCTCG
FIX RACE_95_3 RACE_95_8 RACE_95_11	AGTTCAGCGTGCGGCTCTTTGCCAACTAGCCTGCGTCA-176346 AGTTCAGCGTGCGGCTCTTTGCCAACTAGCCTGCGTCA AGTTCAGCGTGCGGCTCTTTGCCAACTAGCCTGCGTCA AGTTCAGCGTGCGGCTCTTTGCCAACTAGCCTGCGTCA
В	
FIX 17563	1-CCGCGCGTCATGAGTCCCAAAAACCTGACGCCGTTCTTGACGGCGTTGTGGCTGCTATTG
RACE_95_3	CCGTGCGTCATGAGTCCCAAAAACCTGACGCCGTTCTTGACGGCGTTGTGGCTGCTATTG
RACE_95_8	CCGCGCGTCATGAGTCCCAAAAACCTGACGCCGTTCTTGACGGCGTTGTGGCTGCTATTG
RACE_95_13	CCGCGCGTCATGAGTCCCAAAAACCTGACGCCGTTCTTGACGGCGTTGTGGCTGCTATTG
FIX7	GGTCACAGCCGCGTGCCGCGGGTACGCGCAGAAGAATGTTGCGAATTCATAAACGTCAAC
RACE_95_3	GGTCACAGCCGCGTGCCGCGGGTACGCGCAGAAGAATGTTGCGAATTCATAAACGTCAAC
RACE_95_8	GGTCACAGCCGCGTGCCGCGGGTACGCGCAGAAGAATGTTGCGAATTCATAAACGTCAAC
RACE_95_11	GGTCACAGCCGCGTGCCGCGGGTACGCGCAGAAGAATGTTGCGAATTCATAAACGTCAAC
FIX RACE_95_3 RACE_95_8 RACE_95_11	CACCCGCCGGAACGCTGTTACGATTTCAAAATGTGCAATCGCTTCACCGTCGCGTACGTA

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FIX RACE_95_3 RACE_95_8 RACE_95_11	TTTTTATGATTGTCTGCGTTCTGTGGTGCGTCTGGATTTGTCTCTCGACGTTTCTGATAG TTTTCATGATTGTCTGCGTTCTGTGGTGCGTCTGGATCTGTCTCTCACGTTTCTGATAG TTTTCATGATTGTCTGCGTTCTGTGGTGCGTCTGGATCTGTCTCTCGACGTTTCTGATAG
FIX RACE_95_3 RACE_95_8 RACE_95_11	CCATGTTCCATCGACGATCCTCGGGAATGCCAGAGTAGATTTTCATGAATCCACAGGCTG CCATGTTCCATCGACGATCCTCGGGAATGCCAGAGTAGATTTTCATGAATCCACAGGCTG CCATGTTCCATCGACGATCCTCGGGAATGCCAGAGTAGATTTTCATGAATCCACAGGCTG
FIX RACE_95_3 RACE_95_8 RACE_95_11	CGGTGTCCGGACGGCGAAGTCTGCTACAGTCCCGAGAAAACGGCTGAGATTCGCGGGATC CGGTGTCCGGACGGCGAAGTCTGCTACAGTCCCGAGAAAACGGCTGAGATTCGCGGGATC CGGTGTCCGGACGGCGAAGTCTGCTACAGTCCCCAGAAAACGGCTGAGATTCGCGGGATC CGGTGTCCGGACGGCGAAGTCTGCTACAGTCCCGAGAAAACGGCTGAGATTCGCGGGATC
FIX RACE_95_3 RACE_95_8 RACE_95_11	GTCACCACCATGACCCATTCATTGACACGCCAGGTCGTACACAACAAACTGACGAGCTGC GTCACCACCATGACCCATTCATTGACACGCCAGGTCGTACACAAACAA
FIX RACE_95_3 RACE_95_8 RACE_95_11	AACTACAATCCCTAAGTCTCTTCCTCGAGGGCCTTACAGCCTATGGGAAAGTAAGACAGA AACTACAATCCAACTACAATCCAACTACAATCC
FIX RACE_95_3 RACE_95_8 RACE_95_11	GGGACAAAACATCATTAAAAAAAAAAGTCTAATTTCACGTTTTGTACCCCCCCTTCCCCTC
FIX RACE_95_3 RACE_95_8 RACE_95_11	CGTGTTGTAGGTTATACCTCGAAGCTGACGGCCGAATACGCTGCGGCAAAGTGAACGACAGTTATACCTCGAAGCTGACGGCGAATACGCTGCGGCAAAGTGAACGACAGTTATACCTCGAAGCTGACGGCGAATACGCTGCGGCAAAGTGAACGACAGTTATACCTCGAAGCTGACGGCGAATACGCTGCGGCAAAGTGAACGACA
FIX RACE_95_3 RACE_95_8 RACE_95_11	AGGCGCAGTACCTGCTGGGCGCCGCTGGCAGCGTTCCCTATCGATGGATCAACCTGGAAT AGGCGCAGTACCTGCGCGCCGCTGGCAGCGTTCCCTATCGATGGATCAACCTGGAAT AGGCGCAGTACCTGCGCCCCCTGGCGCGCGTTCCCTATCGATGGATCAACCTGGAAT AGGCGCAGTACCTGCTGGGCGCCCCCTGGCAGCGTTCCCTATCGATGGATCAACCTGGAAT
FIX RACE_95_3 RACE_95_8 RACE_95_11	ACGACAAGATAACCCGGATCGTGGGCCTGGATCAGTACCTGGAGAGCGTTAAGAAACACA ACGACAAGATAACCCGGATCGTGGGCCTGGATCAGTACCTGGAGAGCGTTAAGAAACACA ACGACAAGATAGCCCGGATCGTGGGCCTGGATCAGTACCTGGAGAGCGTTAAGAAACACA ACGACAAGATAACCCGGATCGTGGGCCTGGATCAGTACCTGGAGAGCGTTAAGAAATACA
FIX RACE_95_3 RACE_95_8 RACE_95_11	AACGGCTGGATGTGTGCCGCGCTAAAATGGGCTATATGCTGCAG TGA ATAATAAA-174887 AACGGCTGGATGTGTGCCGCGCTAAAATGGGCTATATGCTGCAG TGA ATAATAAA AACGGCTGGATGTGTGCCGCGCTAAAATGGGCTATATGCTGCAG TGA ATAATAAA AACGGCTGGATGTGTGCCGCGCTAAAATGGGCTATATGCTGCAG TGA ATAATAAA
c	
RACE_95_3 RACE 95 8	CGCTAAAATGGGCTATATGCTGCAG TGA ATAAPAAATGTGTGTTTGTCCGA-174841 CGCTAAAATGGGCTATATGCTGCAG TGA ATAAAAAATGTGTGTTTTGTCC G CAAAAAAAA CGCTAAAATGGGCTATATGCTGCAG TGA ATAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAA

Fig. 4 UL131-128 mRNA processing — Panels (A-C) compare FIX-BAC DNA sequence (numbered according to Chee et al.) to a set of cDNA sequences from RACE clones 95-3, 95-8 and 95-11 (A) UL131 region, (B) UL128 region, (C) UL131-128 transcripts 3' end. Start codons, stop codons and the polyA site are in bold face, mRNA processing signals (splice donor sequence, splice acceptor sequence, AATAAA signal) are grey-shaded.

Figure 5

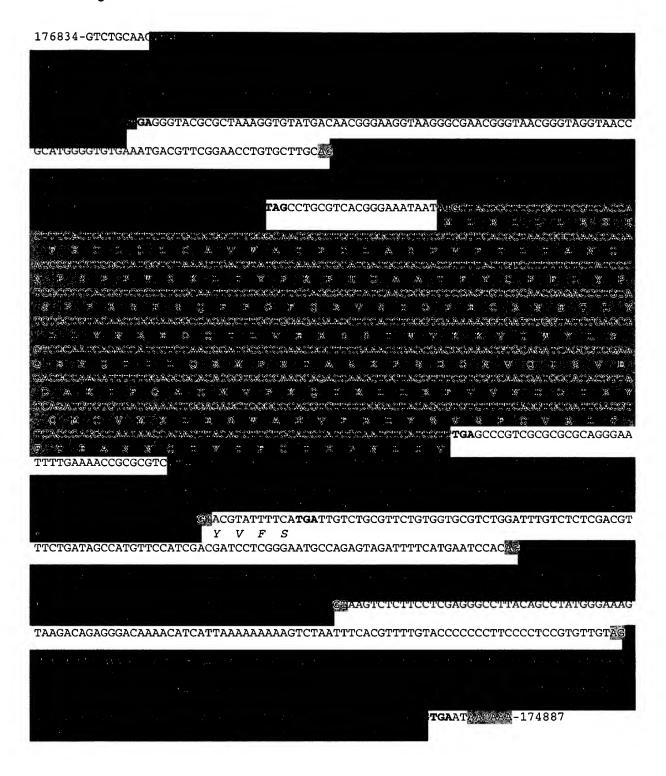


Fig. 5 Exon-intron organization of the FIX-BAC UL131-128 genetic locus. UL131 (green); UL130 (orange); UL128 (blue); UL128x1 C-terminus (light blue).

Figure 6

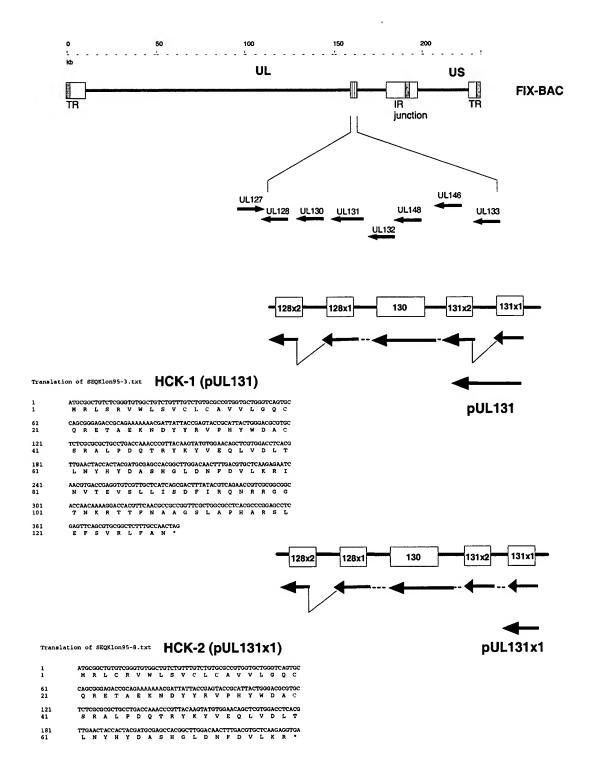
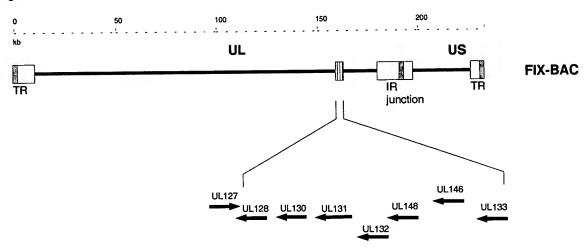
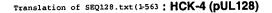
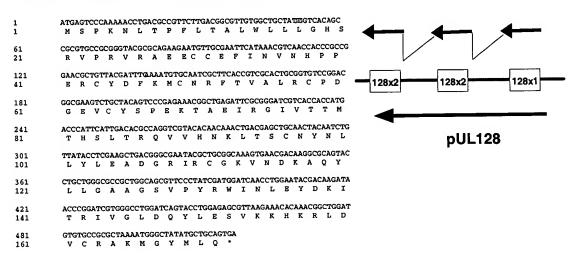


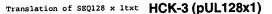
Fig. 6 Scheme of the differentially spliced transcripts of the UL131-128 region. Upper panel RACE clone 95-3 and predicted open reading frame (orf) pUL131 (HCK-1). Lower panel RACE clone 95-8 and predicted orf UL131x1 (HCK-2).











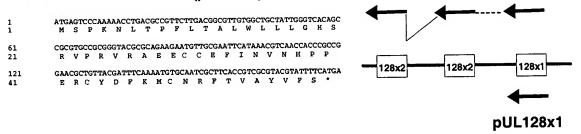


Fig. 7 Scheme of the differentially spliced transcripts of the UL131-128 region. Upper panel SEQUL128B and predicted open reading frame (orf) pUL128 (HCK-4). Lower panel SEQUL128A and predicted orf UL128x1 (HCK-3).

Figure 8

Northern Blot Analys s

RVFIX, **RVFIX** mutants and laboratory strains:

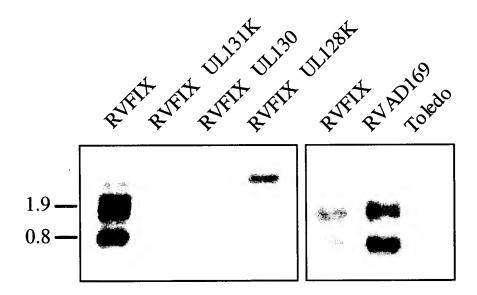


Fig. 8 mRNA was prepared from RVFIX-infected fibroblasts 4 days p.i. using Rneasy Mini, QlAshredder and Oligotex mRNA Mini kits according to the manufacturer's guidance (Qiagen). For Nothern blotting, 1 μ g RNA was electrophoresed on an agarose gel according to the MOPS-formaldehyde protocol and blotted onto Hybond N+ membranes (Amersham Pharmacia). Blots were hybridized with a UL131-128 specific probe.

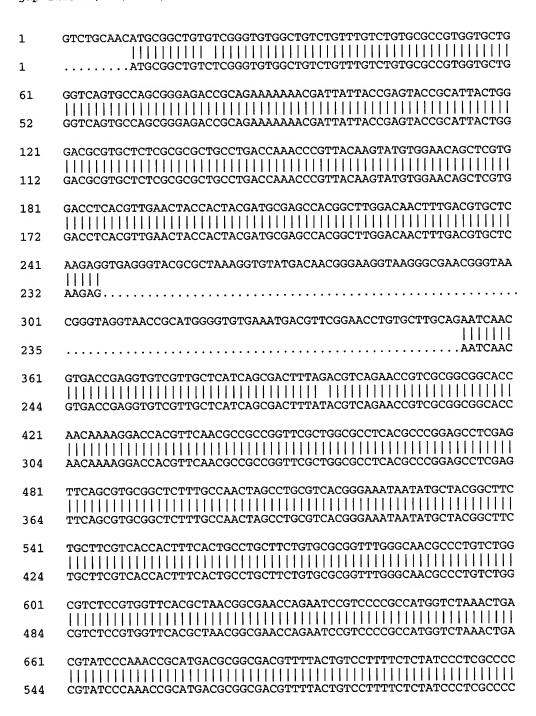
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Figure 9

Comparison RACE clone 95-3 - FIX genomic sequence

Upper line: SEQFIX UL131-128.txt, from 10 to 1977 Lower line: SEQKlon95-3.txt, from 1 to 1741

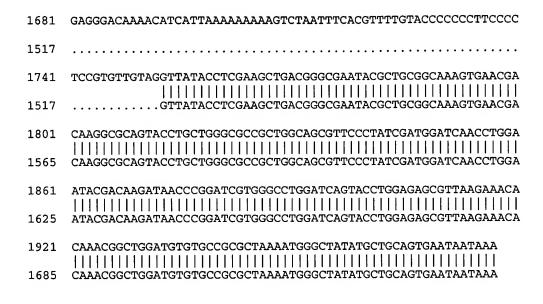
SEQFIX UL131-128.txt:SEQKlon95-3.txt identity= 99.66%(1735/1741)
gap=11.94%(236/1977)



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721 504	CACGGTCCCCTCGCAATTCCCGGGGTTCCAGCGGGTATCAACGGGTCCCGAGTGTCGCA
781	ACGAGACCCTGTATCTGCTGTACAACCGGGAAGGCCAGACCTTGGTGGAGAGAAGCTCCA
664	ACGAGACCCTGTATCTGCTGTACAACCGGGAAGGCCAGACCTTGGTGGAGAAGCTCCA
841	CCTGGGTGAAAAAGGTGATCTGGTATCTGAGCGGTCGCAATCAGACCATCCTCCAACGGA
724	CCTGGGTGAAAAAGGTGATCTGGTATCTGAGCGGTCGCAATCAGACCATCCTCCAACGGA
901	TGCCCCGAACGGCTTCGAAACCGAGCGACGGAAACGTGCAGATCAGCGTGGAAGACGCCA
784	TGCCCCGAACGGCTTCGAAACCGAGCGACGGAAACGTGCAGATCAGCGTGGAAGACGCCA
961	AGATTTTTGGAGCGCACATGGTGCCCAAGCAGACCAAGCTGCTACGTTTCGTCGTCAACG
844	AGATTTTGGAGCGCACATGGTGCCCAAGCAGACCAAGCTGCTACGTTTCGTCGCCAACG
1021	${\tt ATGGCACACGTTATCAGATGTGTGTGATGAAACTGGAGAGCTGGGCCCACGTCTTCCGGG}$
904	ATGGCACACGTTATCAGATGTGTGTGATGAAACTGGAGAGCTGGGCCCACGTCTTCCGGG
1081	ACTACAGCGTGTCTTTTCAGGTGCGATTGACGTTCACCGAGGCCAATAACCAGACTTACA
964	
1141	CCTTCTGCACCCATCCCAATCTCATCGTTTGAGCCCGTCGCGCGCG
1024	
1201	${\tt AACCGCGCGTCATGAGTCCCAAAAACCTGACGCCGTTCTTGACGGCGTTGTGGCTGCTAT}$
1084	AACCGTGCGTCATGAGTCCCAAAAACCTGACGCCGTTCTTGACGGCGTTGTGGCTGCTAT
1261	TGGGTCACAGCCGCGTGCCGCGGGTACGCGCAGAAGAATGTTGCGAATTCATAAACGTCA
1144	
1321	${\tt ACCACCCGCCGGAACGCTGTTACGATTCAAAATGTGCAATCGCTTCACCGTCGCGTACG}$
1204	
1381	${\tt TATTTCATGATTGTCTGCGTTCTGTGGTGCGTCTGGATTTGTCTCTCGACGTTTCTGAT}$
1264	
1441	${\tt AGCCATGTTCCATCGACGATCCTCGGGAATGCCAGAGTAGATTTTCATGAATCCACAGGC}$
1324	AGCCATGTTCCATCGACGATCCTCGGGAATGCCAGAGTAGATTTTCATGAATCCACAGGC
1501	TGCGGTGTCCGGACGCGAAGTCTGCTACAGTCCCGAGAAAACGGCTGAGATTCGCGGGA
1384	TGCGGTGTCCGGACGCGAAGTCTGCTACAGTCCCGAGAAAACGGCTGAGATTCGCGGGA
1561	TCGTCACCACCATGACCCATTCATTGACACGCCAGGTCGTACACAACAAACTGACGAGCT
1444	
1621	GCAACTACAATCCGTAAGTCTCTTCCTCGAGGGCCTTACAGCCTATGGGAAAGTAAGACA
1504	

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Translation of SEQKlon95-3.txt: HCK-1 (pUL131)

1	ATG	CGG	CTG	TCT	CGG	GTG	TGG	CTG	TCT	GTT	TGT	СТG	TGC	GCC	GTG	GTG	CTG	GGT	CAG	TGC
1	M	R	L	S	R	V	W	L	S	V	С	L	С	A	V	V	L	G	Q	С
61	CAG	CGG	GAG	ACC	GCA	GAA	AAA	AAÇ	GAT	тат	TAC	CGA	GTA	CCG	CAT	TAC	TGG	GAC	GCG	TGC
21	Q	R	E	T	A	E	K	N	D	Y	Y	R	V	P	Н	Y	W	D	Α	С
121	TCT	CGC	GCG	CTG	ССТ	GAC	ÇAA	ACC	CGT	TAC	AAG	TAT	GTG	GAA	CAG	CTC	GTG	GAC	CTC	ACG
41	S	R	A	L	P	D	Q	Т	R	Y	K	Y	V	E	Q	L	V	D	L	T
181	TTG	AAC	TAC	CAC	TAC	GAT	GCG	AGC	CAC	GGC	TTG	GAC	AAC	TTT	GAC	GTG	CTC	AAG	AGA	ATC
61	L	Ŋ	Y	Н	Y	D	A	S	Н	G	L	D	N	F	D	٧	L	K	R	I
241	AAC	GTG	ACC	GAG	GTG	TCG	TTG	CTC	ATC	AGC	GAC	ттт	ATA	CGT	CAG	AAC	CGT	'CGC	GGC	GGC
81	Ŋ	V	T	E	V	s	L	L	I	s	D	F	Ι	R	Q	N	R	R	G	G
301	ACC	AAC	'AAA	AGG	ACC	ACG	TTC	AAC	GCC	GCC	GGT	TCG	СТС	GCG	CCT	CAC	GCC	:CGG	AGC	CTC
101	Т	Ŋ	K	R	Т	T	F	N	A	A	G	S	L	A	P	Н	Α	R	S	L
361	GAG	TTC	AGC	GTG	CGG	CTC	TTT	GCC	AAC	TAG	;									
121	E	F	S	V	R	L	F	A	Ŋ	*										

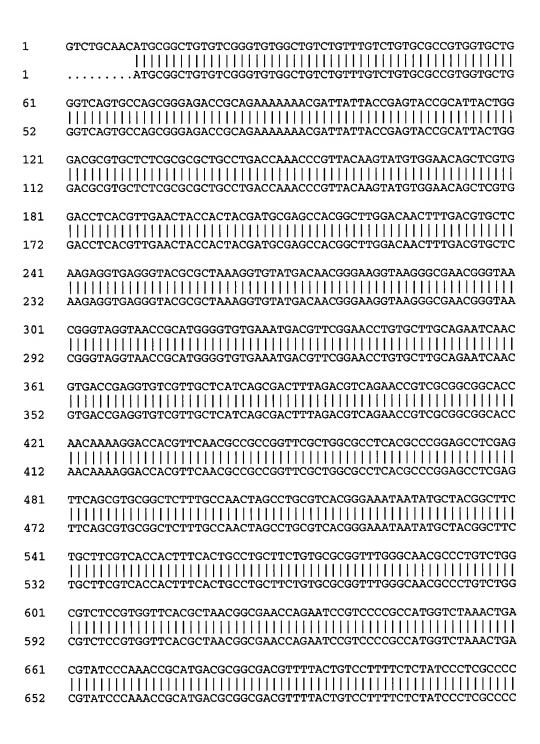
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Figure 10

Comparison RACE clone 95-8 -FIX genomic sequence

Upper line: SEQFIX UL131-128.txt, from 10 to 1977 Lower line: SEQKlon95-8.txt, from 1 to 1849

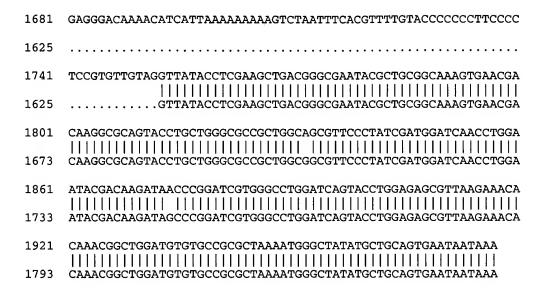
SEQFIX UL131-128.txt:SEQKlon95-8.txt identity= 99.78%(1845/1849) gap=6.47%(128/1977)



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721 712	CACGGTCCCCTCGCAATTCCCGGGGTTCCAGCGGGTATCAACGGGTCCCGAGTGTCGCA
781 772	ACGAGACCCTGTATCTGCTGTACAACCGGGAAGGCCAGACCTTGGTGGAGAGAAGCTCCA
841 832	CCTGGGTGAAAAAGGTGATCTGGTATCTGAGCGGTCGCAATCAGACCATCCTCCAACGGA
901 892	TGCCCCGAACGGCTTCGAAACCGAGCGACGGAAACGTGCAGATCAGCGTGGAAGACGCCA
961 952	AGATTTTTGGAGCGCACATGGTGCCCAAGCAGACCAAGCTGCTACGTTTCGTCGTCAACG
1021 1012	ATGGCACACGTTATCAGATGTGTGATGAAACTGGAGAGCTGGGCCCACGTCTTCCGGG
1081 1072	ACTACAGCGTGTCTTTTCAGGTGCGATTGACGTTCACCGAGGCCAATAACCAGACTTACA
1141 1132	CCTTCTGCACCCATCCCAATCTCATCGTTTGAGCCCGTCGCGCGCG
1201 1192	AACCGCGCGTCATGAGTCCCAAAAACCTGACGCCGTTCTTGACGGCGTTGTGGCTGCTAT
1261 1252	TGGGTCACAGCCGCGTGCCGCGGGTACGCGCAGAAGAATGTTGCGAATTCATAAACGTCA
1321 1312	ACCACCCGCCGGAACGCTGTTACGATTTCAAAATGTGCAATCGCTTCACCGTCGCGTACG
1381 1372	TATTTTCATGATTGTCTGCGTTCTGTGGTGCGTCTGGATTTGTCTCTCGACGTTTCTGAT
1441 1432	AGCCATGTTCCATCGACGATCCTCGGGAATGCCAGAGTAGATTTTCATGAATCCACAGGC
1501 1492	TGCGGTGTCCGGACGGCGAAGTCTGCTACAGTCCCGAGAAAACGGCTGAGATTCGCGGGA
1561 1552	TCGTCACCACCATGACCCATTCATTGACACGCCAGGTCGTACACAAAACTGACGAGCT
1621 1612	GCAACTACAATCCGTAAGTCTCTTCCTCGAGGGCCTTACAGCCTATGGGAAAGTAAGACA

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Translation of SEQKlon95-8.txt: HCK-2 (pUL131x1)

1	ATG	CGG	CTG	TGT	CGG	GTG	TGG	CTG	TCT	GTT	TGT	CTG	TGC	GCC	GTG	GTG	CTG	GGT	CAG	TGC
1	M	R	L	С	R	V	W	L	S	V	С	L	С	A	V	V	L	G	Q	С
61	CAG	CGG	GAG	ACC	GCA	GAA	AAA	AAC	GAT	TAT	TAC	CGA	GTA	CCG	САТ	TAC	TGG	GAC	GCG	TGC
21	Q	R	E	Т	Α	E	K	N	D	Y	Y	R	V	P	H	Y	W	D	A	С
121	TCI	CGC	:GCG	CTG	CCT	GAC	CAA	ACC	CGT	TAC	AAG	TAT	GTG	GAA	CAG	CTC	GTG	GAC	CTC	ACG
41	S	R	A	L	P	D	Q	Т	R	Y	K	Y	V	E	Q	L	V	D	L	T
181	TTG	AAC	TAC	CAC	TAC	GAT	'GCG	AGC	CAC	GGC	TTG	GAC	AAC	TTT	GAC	GTG	CTC	AAG	AGG	TGA
61	, F	N	Y	Н	Y	D	Α	S	H	G	L	D	N	F	D	V	L	K	R	*

Figure 11

Comparison RACE clon 95-11 -FIX genomic sequenc

Upper line: SEQFIX UL131-128.txt, from 10 to 1977 Lower line: SEQKlon95-11.txt, from 1 to 1620

SEQFIX UL131-128.txt:SEQKlon95-11.txt identity= 99.57%(1611/1618) gap=18.24%(361/1979)

1	GTCTGCAACATGCGGCTGTGTCGGGTGTGCTGTTTTGTCTGTGCGCCGTGGTG
1	ATGCGGCTGTCGGGTGTGGCTGTTTGTCTGTGCGCCGTGGTG
61	GGTCAGTGCCAGCGGGAGACCGCAGAAAAAAACGATTATTACCGAGTACCGCATTACT
52	GGTCAGTGCCAGCGGGAGACCGCAGAAAAAAAACGATTATTACCGAGTACCGCATTACT
119	GGGACGCGTGCTCTCGCGCGCTGCCTGACCAAACCCGTTACAAGTATGTGGAACAGCTCG
112	GGGACGCGTGCTCGCGCGCTGCCTGACCAAACCCGTTACAAGTATGTGGAACAGCTCG
179	TGGACCTCACGTTGAACTACCACTACGATGCGAGCCACGGCTTGGACAACTTTGACGTGC
172	TGGACCTCACGTTGAACTACCACTACGATGCGAGCCACGGCTTGGACAACTTTGACGTGC
239	TCAAGAGGTGAGGGTACGCGCTAAAGGTGTATGACAACGGGAAGGTAAGGGCGAACGGGT
232	TCAAGAG
299	AACGGGTAGGTAACCGCATGGGGTGTGAAATGACGTTCGGAACCTGTGCTTGCAGAATCA
237	AATCA
359	ACGTGACCGAGGTGTCGTTGCTCATCAGCGACTTTAGACGTCAGAACCGTCGCGGCGCA
244	ACGTGACCGAGGTGTCGTTGCTCATCAGCGACTTTAGACGTCAGAACCGTCGCGGCGGCA
419	CCAACAAAAGGACCACGTTCAACGCCGCCGGTTCGCTGGCGCCTCACGCCCGGAGCCTCG
304	CCAACAAAAGGACCACGTTCAACGCCGCCGGTTCGCTGGCGCCTCACGCCCGGAGCCTCG
479	AGTTCAGCGTGCGGCTCTTTGCCAACTAGCCTGCGTCACGGGAAATAATATGCTACGGCT
364	AGTTCAGCGTGCGGCTCTTTGCCAACTAGCCTGCGTCACGGGAAATAATATGCTACGGCT
539	TCTGCTTCGTCACCACTTTCACTGCCTGCTTCTGTGCGCGGTTTGGGCAACGCCCTGTCT
424	TCTGCTTCGTCACCACTTTCACTGCCTGCTTCTGTGCGCGGTTTGGGCAACGCCCTGTCT
599	GGCGTCTCCGTGGTTCACGCTAACGGCGAACCAGAATCCGTCCCCGCCATGGTCTAAACT
484	GGCGTCTCCGTGGTTCACGCTAACGGCGAACCAGAATCCGTCCCCGCCATGGTCTAAACT
659	GACGTATCCCAAACCGCATGACGCGGCGACGTTTTACTGTCCTTTTCTCTATCCCTCGCC
544	GACGTATCCCAAACCGCATGACGCGGCGACGTTTTACTGTCCTTTTCTCTATCCCTCGCC

ROTINVELL, FIGG, ERNST & MANBECK Application Serial No.: New Application By: Gabriele HAHN Attorney: Robert B. Murray Attorney Docket No.: 2923-0545 (Figures 1-3 in specification) 14 of 20

719 604	CCCACGGTCCCCTCGCAATTCCCGGGGTTCCAGCGGGTATCAACGGGTCCCGAGTGTCG
779	
664	CAACGAGACCCTGTATCTGCTGTACAACCGGGAAGGCCAGACCTTGGTGGAGAGAGCTC
839 724	CACCTGGGTGAAAAAGGTGATCTGGTATCTGAGCGGTCGCAATCAGACCATCCTCCAACG
899	GATGCCCCGAACGGCTTCGAAACCGAGCGACGGAAACGTGCAGATCAGCGTGGAAGACGC
784	
959	CAAGATTTTTGGAGCGCACATGGTGCCCAAGCAGACCAAGCTGCTACGTTTCGTCGTCAA
844	
1019	CGATGGCACACGTTATCAGATGTGTGTGATGAAACTGGAGAGCTGGGCCCACGTCTTCCG
904	
1079	GGACTACAGCGTGTCTTTTCAGGTGCGATTGACGTTCACCGAGGCCAATAACCAGACTTA
964	
1139	CACCTTCTGCACCCATCCCAATCTCATCGTTTGAGCCCGTCGCGCGCG
1024	
1199	AAAACCGCGCGTCATGAGTCCCAAAAACCTGACGCCGTTCTTGACGGCGTTGTGGCTGCT
1084	AAAACCGCGCGTCATGAGTCCCAAAAACCTGACGCCGTTCTTGACGGCGTTGTGGCTGCT
1259	ATTGGGTCACAGCCGCGTGCCGCGGGTACGCGCAGAAGAATGTTGCGAATTCATAAACGT
1144	ATTGGGTCACAGCCGCGTGCCGCGGGTACGCGCAGAAGAATGTTGCGAATTCATAAACGT
1319	CAACCACCGCCGGAACGCTGTTACGATTTCAAAATGTGCAATCGCTTCACCGTCGCGTA
1204	CAACCACCGCCGGAACGCTGTTACGATTTCAAAATGTGCAATCGCTTCACCGTCGC
1379	${\tt CGTATTTCATGATTGTCTGCGTTCTGTGGTGCGTCTGGATTTGTCTCTCGACGTTTCTG}$
1262	
1439	ATAGCCATGTTCCATCGACGATCCTCGGGAATGCCAGAGTAGATTTTCATGAATCCACAG
1262	
1499	GCTGCGGTGTCCGGACGCGAAGTCTGCTACAGTCCCGAGAAAACGGCTGAGATTCGCGG
1262	ACTGCGGTGTCCGGACGCGAAGTCTGCTACAGTCCCGAGAAAACGGCTGAGATTCGCGG
L559	GATCGTCACCACCATGACCCATTCATTGACACGCCAGGTCGTACACAACAAACTGACGAG
L321	GATCGTCACCACCATGACCCATTCATTGACACGCCAGGTCGTACACAACAAACTGACGAG
1619	CTGCAACTACAATCCGTAAGTCTCTTCCTCGAGGGCCTTACAGCCTATGGGAAAGTAAGA
1381	CTGCAACTACAATCT

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1679	CAGAGGGACAAAACATCATTAAAAAAAAAAGTCTAATTTCACGTTTTGTACCCCCCCTTCC
1396	
1739	CCTCCGTGTTGTAGGTTATACCTCGAAGCTGACGGGCGAATACGCTGCGGCAAAGTGAAC
1396	GTTATACCTCGAAGCTGACGGCGAATACGCTGCGGCAAAGTGAAC
1799	GACAAGGCGCAGTACCTGCTGGGCGCCGCTGGCAGCGTTCCCTATCGATGGATCAACCTG
1442	GACAAGGCGCAGTACCTGCTGGGCGCCGCTGGCAGCGTTCCCTATCGATGGATCAACCTG
1859	GAATACGACAAGATAACCCGGATCGTGGGCCTGGATCAGTACCTGGAGAGCGTTAAGAAA
1502	GAATACGACAAGATAACCCGGATCGTGGGCCTGGATCAGTACCTGGAGAGCGTTAAGAAA
1919	CACAAACGGCTGGATGTGTGCCGCGCTAAAATGGGCTATATGCTGCAGTGAATAATAAA
1562	TACAAACGGCTGGATGTGTGCCGCGCTAAAATGGGCTATATGCTGCAGTGAATAATAAA

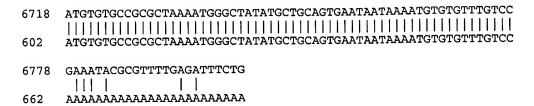
Figure 12

Comparison SEQ 128 B - FIX genomic sequence

Upper line: FIX genomic sequence Lower line: SEQ 128 B

5998	ATGAGTCCCAAAAACCTGACGCCGTTCTTGACGGCGTTGTGGCTGCTATTGGGTCACAGC
1	ATGAGTCCCAAAAACCTGACGCCGTTCTTGACGGCGTTGTGGCTGCTATTGGGTCACAGC
6058	CGCGTGCCGCGGGTACGCGCAGAAGAATGTTGCGAATTCATAAACGTCAACCACCCGCCG
61	
6118	GAACGCTGTTACGATTTCAAAATGTGCAATCGCTTCACCGTCGCGTACGTA
121	
6178	TTGTCTGCGTTCTGTGGTGCGTCTGGATCTGTCTCTCGACGTTTCTGATAGCCATGTTCC
181	TTGTCTGCGTTCTGTGGTGCGTCTGGATCTCTCTCGACGTTTCTGATAGCCATGTTCC
6238	ATCGACGATCCTCGGGAATGCCAGAGTAGATTTTCATGAATCCACAGGCTGCGGTGTCCG
241	
6298	GACGGCGAAGTCTGCTACAGTCCCGAGAAAACGGCTGAGATTCGCGGGATCGTCACCACC
301	GACGGCGAAGTCTGCTACAGTCCCGAGAAAACGGCTGAGATTCGCGGGATCGTCACCACC
6358	ATGACCCATTCATTGACACGCCAGGTCGTACACAACAAACTGACGAGCTGCAACTACAAT
361	
6418	CCGTAAGTCTCTTCCTCGAGGGCCTTACAGCCTATGGGAAAGTAAGACAGAGGGACAAAA
421	cc
6478	${\tt CATCATTAAAAAAAAAGTCTAATTTCACGTTTTGTACCCCCCCTTCCCCTCCGTGTTGTA}$
423	
6538	GGTTATACCTCGAAGCTGACGGCGAATACGCTGCGGCAAAGTGAACGACAAGGCGCAGT
423	.GTTATACCTCGAAGCTGACGGCGAATACGCTGCGGCAAAGTGAACGACAAGGCGCAGT
6598	ACCTGCTGGGCGCCGCTGGCGCGTTCCCTATCGATGGATCAACCTGGAATACGACAAGA
482	
6658	TAGCCCGGATCGTGGGCCTGGATCAGTACCTGGAGAGCGTTAAGAAACACAAACGGCTGG
542	TAGCCCGGATCGTGGGCCTGGATCAGTACCTGGAGAGCGTTAAGAAACACAAACGGCTGG

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Translation of SEQ128 B x 1.txt: HCK-3 (pUL128x1)

1	ATG	AGT	CCC	AAA	AAC	CTG.	ACG	CCG'	TTC	TTG.	ACG	GCG	TTG	TGG	CTG	CTA	TTG	GGT	CAC	AGC
1	М	S	P	K	N	L	T	P	F	L	T	A	L	W	L	L	L	G	Н	S
61	CGC	GTG	CCG	CGG	GTA	CGC	GCA	GAA	GAA	TGT	TGC	GAA	TTC	ATA	AAC	GTC	AAC	CAC	CCG	CCG
21	R	V	P	R	V	R	A	E	E	С	С	E	F	I	Ŋ	V	Ŋ	Н	P	P
121	GAA	.CGC	TGT	TAC	GAT	TTC	AAA	ATG	TGC	ААТ	CGC	TTC	ACC	GTC	GCG	TAC	GTA	ттт	TCA'	TGA
41	E	R	C	Y	D	F	K	M	С	Ŋ	R	F	T	V	Α	Y	V	F	S	*

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Figure 13

Comparison SEQ 128 A - FIX genomic sequence

Upper line: FIX-BAC Lower line: SEQ128 A

5998 1	ATGAGTCCCAAAAACCTGACGCCGTTCTTGACGGCGTTGTGGCTGCTATTGGGTCACAGC
6058 61	CGCGTGCCGCGGTACGCGCAGAAGAATGTTGCGAATTCATAAACGTCAACCACCCGCCG
6118 121	GAACGCTGTTACGATTTCAAAATGTGCAATCGCTTCACCGTCGCGTACGTA
6178	${\tt TTGTCTGCGTTCTGGGTGCGTCTGGATTTGTCTCTCGACGTTTCTGATAGCCATGTTCC}$
166	
6238	ATCGACGATCCTCGGGAATGCCAGAGTAGATTTTCATGAATCCACAGGCTGCGGTGTCCG
166	
6298 178	GACGGCGAAGTCTGCTACAGTCCCGAGAAAACGGCTGAGATTCGCGGGATCGTCACCACC
6358 238	ATGACCCATTCATTGACACGCCAGGTCGTACACAACAACTGACGAGCTGCAACTACAAT
6418 298	CCGTAAGTCTCTTCCTCGAGGGCCTTACAGCCTATGGGAAAGTAAGACAGAGGGACAAAA
6478	CATCATTAAAAAAAAAGTCTAATTTCACGTTTTGTACCCCCCCTTCCCCTCCGTGTTGTA
300	
6538 300	GGTTATACCTCGAAGCTGACGGGCGAATACGCTGCGGCAAAGTGAACGACAAGGCGCAGT
6598 359	ACCTGCTGGGCGCCGCTGGCAGCGTTCCCTATCGATGGATCAACCTGGAATACGACAAGA
6658 419	TAACCCGGATCGTGGGCCTGGATCAGTACCTGGAGAGCGTTAAGAAACACAAACGGCTGG
6718 479	ATGTGTGCCGCGCTAAAATGGGCTATATGCTGCAGTGAATAATAAAATGTGTGTTTTGTCC

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Translation of SEQ128 A: HCK-4 (pUL128)

1	ATG	ልርሞር	ccci	AAA	AACC	TGA	ACGO	CGI	TCI	TG	ACGO	GCG1	TGT	GGG	CTGC	TAT	rtgo	GT(CACA	AGC
1	М	S		K	N	L	T	P	F	L	Т	A	L	W	L	L	L	G	Н	S
61	CGC	стс	CCG	~GG(TTAC	CGCC	CAC	SAAC	CAAE	'GT'	rgco	CAAC	rTC <i>I</i>	ATA	AAC	STC	AAC	CAC	CCGC	CCG
21	R		P	R	V	R		E				E	F	I	Z	V	Ŋ	H	P	P
121	GAA	CGC	ጥርጥ	TAC	GAT	rrc <i>i</i>	AAA	ATG:	rgcz	YAT	CGC!	rtc <i>i</i>	ACC	3TC	GCA(CTG	CGG'	rgt(CCG	GAC
41	E	R		Y	D	F	K			N	R	F	Т	V	A	L	R	С	P	D
181	GGC	CAA	GTC'	тсс	TAC	AGTO	ccc	GAG	AAA	CGG	CTG	AGA!	rtc	3CG	GGA'	rcg'	TCA	CCA	CCA'	rg
61	G	E	V	C	Y	s	P	E	K	Т	A	E	I	R	G	I	V	T	Т	M
241	ACC	_' '' ב	ጥር ል	ጥጥር፥	ACA	CGC	CAG	GTC	GTA	CAC.	AAC.	AAA	CTG.	ACG.	AGC'	TGC.	AAC	TAC.	AAT	CTG
81	Т	Н			T	R				H	N	K		Т	S	С	Ŋ	Y	Ŋ	L
301	01 TTATACCTCGAAGCTGACGGGCGAATACGCTGCGGCAAAGTGAACGACAAGGCGCAGTAC																			
101		Y		E	A	D	G	R			С		K	V	Ŋ	D	K	A	Q	Y
361	CTC	יכייים	ccc	GCC	GCT	GGC	AGC	GTT	CCC	тат	CGA	TGG.	ATC	AAC	CTG	GAA	TAC	GAC	AAG	ATA
121		L		A			s	V			R	W	I	Ŋ	L	E	Y	D	K	I
421	ACC	ירכפ	יאיר:	стс	GGC	СТС	GAT	CAG	TAC	CTG	GAG	AGC	GTT	AAG	AAA	CAC	AAA	.CGG	CTG	GAT
141	Т	R	I	V	G	L	D	Q	Y	L	E	S	V	K	K	Н	K	R	L	D
481	81 GTGTGCCGCGCTAAAATGGGCTATATGCTGCAGTGA																			
161	V	C	R	A	K	М	G	Y	M	L	Q	*								

Figure 14

Translation of SEQUL130: HCK-5 (pUL130)

1	ATGCTACGGCTTCTGCTCACCACTTTCACTGCCTGCTTCTGTGCGCGGTTTGGGCA
1	MLRLLLRHHFHCLLLCAVWA
61	ACGCCCTGTCTGGCGTCTCCGTGGTTCACGCTAACGGCGAACCAGAATCCGTCCCCGCCA
21	T P C L A S P W F T L T A N Q N P S P P
121	TGGTCTAAACTGACGTATCCCAAACCGCATGACGCGGCGACGTTTTACTGTCCTTTTCTC
41	W S K L T Y P K P H D A A T F Y C P F L
181	TATCCCTCGCCCCACGGTCCCCCTCGCAATTCCCGGGGTTCCAGCGGGTATCAACGGGT
61	Y P S P P R S P S Q F P G F Q R V S T G
241	CCCGAGTGTCGCAACGAGACCCTGTATCTGCTGTACAACCGGGAAGGCCAGACCTTGGTG
81	P E C R N E T L Y L L Y N R E G Q T L V
301	GAGAGAAGCTCCACCTGGGTGAAAAAGGTGATCTGGTATCTGAGCGGTCGCAATCAGACC
101	ERSSTWVKKVIWYLSGRNQT
361	ATCCTCCAACGGATGCCCCGAACGGCTTCGAAACCGAGCGACGGAAACGTGCAGATCAGC
121	I L Q R M P R T A S K P S D G N V Q I S
421	GTGGAAGACGCCAAGATTTTTGGAGCGCACATGGTGCCCAAGCAGACCAAGCTGCTACGT
141	V E D A K I F G A H M V P K Q T K L L R
481	TTCGTCGTCAACGATGGCACACGTTATCAGATGTGTGTGATGAAACTGGAGAGCTGGGCC
161	F V V N D G T R Y Q M C V M K L E S W A
541	CACGTCTTCCGGGACTACAGCGTGTCTTTTCAGGTGCGATTGACGTTCACCGAGGCCAAT
181	HVFRDYSVSFQVRLTFTEAN
601	AACCAGACTTACACCTTCTGCACCCATCCCAATCTCATCGTTTGA
201	NQTYTFCTHPNLIV*